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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,364	06/01/2001	Ole Thastrup	3759-0107P	3969

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/872,364	Thastrup et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12, 14, 18-21, 23, and 26-64* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12, 14, 18-21, 23, and 26-64* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election without traverse of Group I, drawn to nucleic acids encoding GFP or GFP fusion proteins.

2. Claims 13, 15-17, 22, 24 and 25 have been canceled. Claims 14 and 23 have been amended. Claims 26-34 have been added. Claims 1-12, 14, 18-21, 23 and 26-34 are pending and examined on the merits.

Claim Objections

3. Claims 33 and 34 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 20 and 21, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Specification

4. The disclosure is objected to because of the following informalities: .

The specification is objected to as not complying with 1.821(d) of the Sequence Rules and Regulations. When the specification of a patent application discusses a polypeptide that is set forth in the "Sequence Listing" in accordance with paragraph (c) of the Sequence Rules and

Regulations, reference must be made to the sequence by use of the assigned identifier, in the text of the description. The specification repeatedly cites the clones F64L-Y66-GFP, F64L-GFP, F64L-S65T-GFP and GFP which are SEQ ID NO:16, 18, 20 and 22 respectively.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-12, 14, 18-21, 23 and 26-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 18 recite the limitation of "increased fluorescence...relative to" the GFP of SEQ ID NO:22. It is unclear if the "increased fluorescence" refers to the intensity of the emission at the identical emission maxima of SEQ ID NO:22, or encompasses emission maxima of any wavelength. For purpose of examination, all alternatives will be considered.

Claims 18 and 19 recite "position 1" preceding the chromophore without defining the location of said chromophore. The specification teaches that the chromophore consists of amino acid residues 65-67 in wild-type GFP. However, some of the prior art defined the chromophore as consisting of amino acid residues 64-69 (Inouye et al, FEBS Letters, 1994, Vol. 341, pp. 277-280, Figure 1). Therefore, the recitation of "chromophore"without specifically reciting amino

acid residue numbers renders the claims indefinite. For purpose of examination, the chromophore will be defined as residues 65-67. Furthermore, the recitation of position 1 before the chromophore is undefined. The ordinary meaning of the term "before" in the context of an amino acid sequence refers to residues which are closer to the amino terminus that the referenced position. Thus, position 1 before the chromophore can read on any amino acid which is closer to the N terminus than residue 65. Thus, the metes and bounds of "position 1" cannot be determined.

The recitation of functional GFP analogue in claim 14 lacks antecedent basis in claim 1.

Claim 14 recites "GFP or a functional analog according to claim 1" . Nether the specification nor the claims sets forth the requirements for a "functional analog". It is unclear if claims 14 and 23 encompass variants of SEQ ID NO:22 that are wider in scope then the genus of variants encompassed by claims 1 and 18. Further, it is unclear if the limitations of claims 1 and 18 are incorporated into the nucleotide sequence encoding the GFP of claims 14 and 23. For purpose of examination, all of the above alternatives will be considered.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 14, 18-21, 23, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A)As drawn to claim 14

Claim 14 is drawn in part to a nucleic acid molecule comprising a nucleotide sequence encoding a protein of interest fused to a nucleotide sequence encoding a functional GFP analogue of claim 1. When given the broadest reasonable interpretation, as set forth under the rejection of 112 second paragraph above, the claim encompasses variants of the amino acid sequence of SEQ ID NO:22 that are potentially broader in scope than the variants defined by claim 1. As "functional analogs" are not defined by the specification or the claims, the ordinary meaning of the term, encompassing any sequence variant of SEQ ID NO:22 that would exhibit a fluorescence. Thus, claim 14 is drawn to a genus of proteins. The specification sets forth the specific variants of SEQ ID NO:22 as SEQ ID NO:16, 18 and 20, wherein said variants exhibit an increase in intensity of light emission relative to GFP. However, it is unclear if SEQ ID NO:16, 18 and 20 qualify as "functional analogues" of claim 1 for the reasons set forth in the rejection under 112, second paragraph, above. Therefore, one of skill in the art is unable to discern the structural and functional properties of individual molecules which make up the claimed genus. The specification does not teach a representative number of molecules which would exemplify a functional analogue of SEQ ID NO:16, 18 and 20, therefore the disclosure of a SEQ ID NO:16, 18 and 20 is not sufficient to support claims to a genus of functional analogs.

(B)As drawn to claims 18-23 and 26-34.

Claim 18 is drawn to a functional analogue comprising the amino acid sequence which is modified by at least an amino acid substitution at position 1 preceding the chromophore. For the reasons sated in the rejection under 112, second paragraph above, the claim in interpreted to read on an amino acid substitution being closer to the N terminus that residue 65. Therefore this is a genus claim encompasses amino acid substitutions from residues 1-64 in addition to other substitutions following residue 67. The specification states that only one residue can be sacrificed from the amino terminus of GFP and no more than 15 residues can be deleted from the carboxyl terminus before fluorescence is lost (page 3, lines 26-29). However, no limitations are set forth in the specification or the claims limiting the number of amino acid substitutions which can be made. The specifications describes amino acid substitutions at residues 64 and 66. The general knowledge in the art regarding GFP fluorescence does not provide any indication of how mutation of residues 66 and 64 is affected by mutations in other positions in the full length sequence. It is reasonable to assume that the chromophore at residues 65-67 interacts with the other amino acids withing the protein as the art and the specification teaches that the presence of the last 15 carboxyl terminal amino acids, as well as the N-terminal amino acids(with the exception of the first residue) are necessary for fluorescence. Thus, SEQ ID NO:16, 18 and 20 do not adequately define the claimed genus encompassing numerous amino acid substitutions. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 14, 18, , 20, 21, 23, 33 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Chalfie et al (US 5,491,084).

Claims 14 and 23 are both drawn in part to a nucleic acid molecule comprising a nucleotide sequence encoding a protein of interest fused to a nucleotide sequence encoding GFP. Claim 18 is drawn in part to a nucleic acid molecule comprising a nucleotide sequence encoding a GFP. Claims 20 and 33 are drawn to an expression vector comprising the nucleic acid molecule of claim 18 wherein said nucleic acid molecule is operatively linked to suitable expression control sequences. Claims 21 and 34 are drawn to a recombinant host cell comprising and expression vector that comprises suitable expression control sequences that are operatively linked to the nucleic acid molecule of claim 18.

Chalfie et al discloses a DNA molecule comprising a suitable regulatory element operatively linked to the DNA encoding the GFP from A victoria (column 4, line 65 to column 5, line 10). Chalfie et al further disclose the linkage of the DNA encoding the GFP protein with the DNA encoding a protein of interest (column 4, lines 30-45 and lines 52-54 and column 5, lines

23-29). Chlafie et al disclose host cells comprising said expression vector (column 5, lines 12-20 and column 6, lines 59-61).

11. Claim 14 is rejected under 35 U.S.C. 102(e) as being anticipated by Tsein et al (US 5,625,048).

Claim 14 is drawn in part to a nucleic acid molecule comprising a nucleotide sequence encoding a protein of interest fused to a nucleotide sequence encoding a functional analogue of GFP. Tsein et al disclose a nucleic acid molecule comprising a DNA encoding a functional analog of GFP fused to a protein of interest (claims 15-17).

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

13. Claims 1-3, 8, 9, 10, 11, 12, 18-21, 26, 27, 28, 29, 33 and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-15 of copending Application No. 09/619,310. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '310 application anticipate the instant claims drawn to SEQ ID NO:16, 18 and 20 as well as instant claim 18, drawn to a nucleic acid molecule comprising a nucleotide sequence encoding a functional analogue of a green fluorescent protein having the sequence of SEQ ID NO:22 which has been modified by at lest an amino acid substitution at position 1 preceding the chromophore.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

January 13, 2003